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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,617	06/25/2003	Hui Chen	038602-1585	2499

22428 7590 06/17/2005

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EXAMINER	
SACKEY, EBENEZER O	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,617	CHEN ET AL.	
	Examiner	Art Unit	
	EBENEZER SACKEY	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,32,36-39 and 44-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,32,36-39 and 44-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-4, 32, 36-39 and 44-54 are pending.

Claims 5-31, 33-35 and 40-43 have been cancelled.

Information Disclosure Statement

Receipt of the Information Disclosure Statement filed 11/03/03 and 05/21/04 respectively is acknowledged. Signed copies of the 1449 are attached herewith.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Objections

Applicant is advised that should claim 2 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Note that M13 is identical to M13, when each of R_1 and R_2 is OH and R_3 is hydrogen.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32 and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

1) Nature of invention.

2) State of prior art.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

4) Level of predictability in the art.

5) Amount of direction and guidance provided by the inventor.

6) Existence of working examples.

7) Breadth of claims.

8) Level of ordinary skill in the art.

See below:

In the instant case, applicants are claiming various methods of using compounds of claim 1 e.g., in treating cell proliferation.

1) Nature of the invention.

The nature of the invention is the treatment of tyrosine kinase receptor mediated diseases, treatment of cell proliferation (claims 32, 37). The diseases to be treated include all cancers as well as the presently claimed proliferation treatments. A cell proliferation disease can be abnormal cellular proliferation, continued normal growth after cessation of the triggering stimulus, normal tissue growth lacking partial or complete structural organization, or normal tissue growth not integrated into the surrounding tissue. This term would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by *Helicobacter pylori* infection of ulcers, and the increased epidermal cell turnover induced by *Pipyrosporum ovale* colonization, which causes dandruff. Thus, the claims are very broad.

2) State of the prior art and the predictability or lack thereof in the art.

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibited the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles

establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instantly claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The notion that a substituted tyrphostin derivative of formula (I) that are HER2 and EGFR receptor antagonists, the activity relied on herein, have such a range of uses is not seen in the art at the time of applicants effective filing or even in the present.

The advent of molecular cloning provided additional discrimination within the tyrosine receptor family ultimately revealing the existence of other families containing several distinct receptors based on primary sequence, pharmacology and signal transduction pathways.

Thus, in the absence of a showing of correlation between all the diseases claimed as capable of being treated, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds of claim 1 due to the unpredictability of the role of tyrosine kinase receptor is being mediated.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would be unable to treat or prevent any and all diseases mediated by tyrosine kinase receptors.

4) Level of predictability in the art.

The art pertaining to the treatment remains highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is found on page 44-56 wherein *in vitro* expression of a receptor is provided. However, that embraces a myriad of diseases present in most animal tissues, for example brain. In addition, the gap between *in vitro* activity and *in vivo* utility is large enough to warrant thorough and compelling *in vivo* or clinical data.

6) Existence of working examples.

As discussed above, working example is found on pages 44-56 wherein *in vitro* expression of a receptor is provided. Applicant's limited working example does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention. At best, the treatment currently asserted for the instant invention is breast carcinomas.

7) Breadth of claims.

Claims 32 and 37 are extremely broad due to the vast number of possible diseases encompassed by the instant invention.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the treatment of any tyrosine kinase mediated disease. As a result, necessitating one of ordinary skill in the art to perform an exhaustive search for which diseases can be treated or prevented by compounds of claim 1 in order to practice the claimed invention.

Genentec Inc. V. *Novo Nordisk A/S* (CAFC) 42 USPQ 2D 1001, states that:

"a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds encompassed in instant claim 1, with no assurance of success.

This rejection can be overcome by deleting the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 32, 36, 37, 46, 49 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. In claims 4, 46, 49 and 52, M13 and M24 have not been defined. Claims must, under modern practice, stand alone to define an invention, and incorporation into

claims by express reference to the specification is not permitted. *Ex parte Fressola*, 27 USPQ 2d. 1608, (1993).

2. In claim 32, it is not entirely clear what the compounds and definitions are. It appears that the second compound (page 5 of the preliminary amendment filed 6/25/03) was superimposed onto the definitions of the first compound. Correction is required.

3. Claims 36 and 37 are dependent on cancelled claims 30 and 31 respectively.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al., (WO 95/24190) and Ohmichi et al., The tyrosine Kinase Inhibitor Tyrphostin Blocks the Cellular Actions of Nerve Growth Factor, Biochemistry, Vol. 32, pages 4650-4658, 1993.

Applicants claim a composition comprising structural compound shown in claim 1.

Chen et al., disclose an identical compound. See page 74, lines 17-30. Also see page 4652 (AG1007) and page 4653 1007 of Ohmichi et al.,

Claim Rejections - 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-4 and 32, 36-39 and 44-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., (WO 95/24190).

Applicants claim a protein Kinase inhibitor composition comprising compounds shown in claim 1, wherein the substituents are as defined and their use in treating various cell proliferation.

Determination of the scope and content of the prior art (MPEP §2141.01)

Chen et al., disclose a protein Kinase inhibitor with similar utility (i.e. treating cell proliferation). See the entire reference, especially page 74, lines 16-29, claims 32, 36, 37, 38 and 39.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the composition of the prior art and the composition instantly claimed is that of generic description. The indiscriminate selection of "some" among "many" is *prima facie* obvious. *In re Lemin,* 141 USPQ 814 (1964).

Finding of prima facie obviousness---rational and motivation (MPEP §2142-2143)

The motivation to make the claimed composition derives from the expectation that compositions containing structurally similar compounds would possess similar activity (i.e., anti-proliferation activity).

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art to prepare a protein kinase inhibitor composition as disclosed by Chen et al., with reasonable expectation of success absent a showing of unexpected results and/or yield. Therefore, at the time of filing this application, one of ordinary skill in the art in

possession of Chen et al., would have been in possession of the instant composition and method of use absent a showing of unexpected results and/or properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. Sackey whose telephone number is (571) 272-0704. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

EOS
June 9, 2005

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